Microbicide Trials:
Challenges and Opportunities

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Women and HIV

- **New UNAIDS numbers**
  - Globally, 15.4 million women living with HIV, and the proportion of new HIV infections in women continues to rise

- **Face of HIV increasingly female, young**
  - In Sub-Saharan Africa, young women 15-24 up to 3 times more likely to acquire HIV than men

- **Married, monogamous women at high risk**
  - India: 22% of HIV cases in housewives with single partner
  - In Uganda 50% of new infections within marriage
Women’s Vulnerability to HIV

- Biological, economic and socio-cultural factors:
  - Male-to-female transmission higher
  - Young women at even higher risk
  - Financial dependence on male partners
  - Inequality of women (exploitation and violence)
  - Cultural practices such as early marriages, intergenerational sex and marital infidelity
  - Paradoxically higher HIV rates seen in higher economic index women who live in urban areas
Why Test Microbicides in Developing Countries?

- Countries in greatest need of new HIV prevention options
  - Communities with high HIV incidence
  - Risk-benefit determination can only be obtained where the disease in question is endemic

- Test microbicides in contexts in which they will be used
  - Effectiveness, risk, and adverse events must be studied in relevant populations
  - Clinical and regulatory implications explored and prepared for

- Building understanding and support towards future access from a range of stakeholders
<table>
<thead>
<tr>
<th>Challenges</th>
<th>Opportunities</th>
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<tbody>
<tr>
<td><strong>Microbicide trials</strong></td>
<td>• Conduct epi studies</td>
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<tr>
<td>• Unknown HIV incidence</td>
<td>• Ethics guidelines/community engagement</td>
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<tr>
<td>• True informed consent</td>
<td>• Family planning/condoms</td>
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<td>• Potential social harms</td>
<td>• Referral networks/partnerships</td>
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<td>• High pregnancy rates</td>
<td>• Site development/staff training</td>
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<td>• Long-term ARV treatment</td>
<td>• Capacity building/development of clinical research guidelines</td>
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<td><strong>Resource limitations</strong></td>
<td>• Relationship/trust building</td>
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<tr>
<td>• Clinical infrastructure</td>
<td></td>
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<td>• Ethics and regulatory</td>
<td></td>
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<td><strong>External environment</strong></td>
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<tr>
<td>• Politics, culture, media</td>
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Capacity Building at Research Centres

- Community engagement – establish CAB
- Referral networks for medical care/support
- Infrastructure and equipment
  - Build/purchase/lease and renovate space
  - Acquire medical and office equipment
- Staff development
  - Hire 15-20 per site with diverse expertise
  - Provide GCP, GCLP & study-specific training
- Communications, messaging and tools
- Financial management support
Strengthened or established capacity at 15 research centers (by end of 2008)

<table>
<thead>
<tr>
<th>Country</th>
<th>Number of research centers</th>
<th>Established new</th>
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<tbody>
<tr>
<td>South Africa</td>
<td>9</td>
<td>6</td>
</tr>
<tr>
<td>Kenya</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Rwanda</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Tanzania</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Malawi</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>15</strong></td>
<td><strong>10</strong></td>
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KCMC, Moshi, Tanzania

New infrastructure and equipment → HIV incidence study completed
Clinical studies ongoing
Projet Ubuzima, Kigali, Rwanda

Completed IPM 003 dapivirine gel safety trial

HIV incidence studies ongoing Clinical trials planned
Ladysmith, KwaZulu-Natal, South Africa

Site selection & renovation
Staff selection & training

HIV incidence study ongoing
Clinical trials planned
Ethical Guidelines for Clinical Trials

Many studies taking place in developing countries

Key issues
- Community engagement
- Informed consent process
- Risk reduction counseling
- Family planning
- Management of pregnancy
- STI screening and treatment
- Testing positive at screening
- Participants who seroconvert
- Treatment for physical harms
- Services for study staff
- Post-trial access to products

Guidelines
- UNAIDS/WHO ethical guidelines in HIV prevention trials, 2007
- UNAIDS/AVAC good participatory practices, 2007
- South Africa GCP, 2006
- IPM ethical guidelines, 2006
- Nuffield Council on Bioethics, 2005
- GCM consensus points, 2005
- CIOMS biomedical guidelines, 2002
- WMA Declaration of Helsinki, 2000
- ICH GCP, 1996
Addressing Key Issues

- **HIV transmission**
  - Risk reduction counseling – at screening and during trial
    - Provision of male/female condoms
  - STI screening and treatment – also suggest to partners

- **Pregnancy**
  - Must be on stable form of contraception
    - Prior to study start and throughout study
    - Family planning counseling
  - If fall pregnant, continue with safety evaluation visits
    - Monitoring of pregnancy and baby up to one year
    - Referral to antenatal clinics
    - Pregnancy registry
    - If also seroconverted, referral for PMTCT

- **Disease progression**
  - Not specifically addressed in microbicide trials
    - May refer to acute infection protocols
    - Conduct follow up studies to assess resistance
Provisions for Participants Who Seroconvert During Trials

Microbicide field committed to providing appropriate HIV-related care and ARV therapy

- Implementing in multiple ways:
  - Guided referrals for HIV care, treatment, support
  - Pre-established partnerships with national/local institutions
  - Dedicated financing if national programs cannot sustain
  - Follow-up study protocols (for ARV microbicides)
  - Pursuing additional support from global donors
  - Advocacy for treatment scale up
Key Challenges

- **Timeframe:** participants may not need treatment until years after a trial

- **Migration:** how to ensure access for people who move out of the area or country

- **Follow-up:** how best to keep in touch with participants & inform them of choices

- **Referral networks:** how to ensure their strength over time

- **Sustainability of appropriate long-term Rx**